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EXAMINER

LAM, ANN Y

ART UNIT	PAPER NUMBER
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1641

NOTIFICATION DATE	DELIVERY MODE
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ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/715,017	Applicant(s) MAJUMDAR ET AL.	
	Examiner ANN Y. LAM	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 July 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 64-89 and 92-114 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 64-89 and 92-114 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>9/21/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 110-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sofield et al. (US 2002/0072127) (hereinafter "Sofield") in view of Ellerbrock et al. (US 6,204,920) (hereinafter "Ellerbrock") and Wohlstadter et al. (US 6,066,448) (hereinafter "Wohlstadter").

As to claim 110, Sofield teaches an array of micro-cantilever structures (i.e., an assembly comprising an array of microsensors; cantilever beam (13) and reflective, paddle (14 and 15), each micro-cantilever structure being immersed in a respective vessel of liquid (i.e., individual fluid cell for each of the microsensors), and each vessel comprising both silicon wafer and a glass bottom surface (i.e., a silicon portion and a glass portion forming the individual fluid cell). See pages 1-2, paragraphs 0010 and 0022; and Figure 3. Sofield also teaches that each micro-cantilever structure has a coating of receptor molecules thereon for identifying specific ligands in a sample solution (i.e., functionalized to deflect when exposed to target molecules). See page 1, paragraphs 0003 and 0004. Sofield further teaches a laser diode (i.e., optical beam

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source) and a quadrant photodiode (i.e., optical detector). See page 2, paragraph 0021 and Figure 2. Sofield teaches a cross strip (15) that is equivalent to the claimed ridge since it prevents the reflective paddle portion (14) from bending. See page 2, paragraph 0019 and Figure 1.

However, Sofield fails to teach that the optical beam source is a single optical beam source configured to simultaneously direct an optical beam onto each of the microsensors in the array of microsensors and that the optical detector is an optical detector array configured to simultaneously detect the position of each of the microsensors.

Ellerbrock teaches a single light source that is multiplexed, in order to address multiple sensors while reducing cost of the system with just one light. See column 2, lines 19-31; column 4, lines 45-67; and Figure 2. In addition, Ellerbrock teaches that the light source can emit laser light. See column 5, lines 38-42.

Wohlstadter teaches a CCD array in order to detect and spatially resolve simultaneous emissions of emitted light. See column 25, lines 38-46.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the laser diode of Sofield with a single light source that is multiplexed, as taught by Ellerbrock, in order to address multiple sensors while reducing cost of the system with just one light source. The advantage of producing an optical system for simultaneously emitting a plurality of light beams without requiring multiple light sources provides the motivation to combine the single light source of Ellerbrock with the apparatus of Sofield. In addition, one of ordinary skill in the art at the time of the

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invention would have had reasonable expectation of success in including the single light source in the apparatus of Sofield, since Sofield teaches laser light sources, and the single light source of Ellerbrock is also a laser light source.

It would have also been obvious to one of ordinary skill in the art at the time of the invention to modify the optical detector of Sofield with the CCD array of Wohlstadter, In order to detect and spatially resolve simultaneous emissions of emitted light. The ability to simultaneously detect signals from a plurality of regions improves the efficiency of multiplexed assays, thereby providing the motivation to combine the teachings of Sofield and Wohlstadter. One of ordinary skill in the art at the time of the invention would have also had a reasonable expectation of success in combining the teachings of Sofield and Wohlstadter since Sofield teaches light detection and the CCD array of Wohlstadter is one type of sensor that can detect light.

As to claim 111, the reflective paddle portion is flat (see figure 1 and 3).

As to claims 112-114, one flat side of element (14) (equivalent to the claimed reflective paddle) is considered to be the top portion of the reflective paddle and the other flat side is equivalent to the bottom portion of the reflective paddle. The cross strip (15) (equivalent to the claimed ridge) is thus "on" or "running around at least" a bottom and top portion of element (14) (reflective paddle).

Claims 64-74, 77- 80, 82-89, 92-102, 105-107 and 109 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sofield et al. (US 2002/0072127) (hereinafter "Sofield") in view of Ellerbrock et al. (US 6,204,920) (hereinafter "Ellerbrock") and Wohlstadter et al. (US 6,066,448) (hereinafter "Wohlstadter"), and further in view of Pfost (6,485,690).

As to claims 64 -68, 70, 71, 78, 92-100, 105, 106, Sofield teaches an array of micro-cantilever structures (13, 14 and 15) (i.e., an assembly comprising an array of microsensors; reflective, flat paddle (14 and 15), each micro-cantilever structure being immersed in a respective vessel of liquid (i.e., individual fluid cell for each of the microsensors), and each vessel comprising both silicon wafer and a glass bottom surface (i.e., a silicon portion and a glass portion forming the individual fluid cell). See pages 1-2, paragraphs 0010 and 0022; and Figure 3. Sofield also teaches that each micro-cantilever structure has a coating of receptor molecules thereon for identifying specific ligands in a sample solution (i.e., functionalized to deflect when exposed to target molecules). See page 1, paragraph s0003 and 0004. Sofield further teaches a laser diode (i.e., optical beam source) and a quadrant photodiode (i.e., optical detector). See page 2, paragraph 0021 and Figure 2.

However, Sofield fails to teach that the optical beam source is a single optical beam source configured to simultaneously direct an optical beam onto each of the microsensors in the array of microsensors and that the optical detector is an optical detector array configured to simultaneously detect the position of each of the microsensors.

Ellerbrock teaches a single light source that is multiplexed, in order to address multiple sensors while reducing cost of the system with just one light. See column 2, lines 19-31; column 4, lines 45-67; and Figure 2. In addition, Ellerbrock teaches that the light source can emit laser light. See column 5, lines 38-42.

Wohlstadter teaches a CCD array in order to detect and spatially resolve simultaneous emissions of emitted light. See column 25, lines 38-46.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the laser diode of Sofield with a single light source that is multiplexed, as taught by Ellerbrock, in order to address multiple sensors while reducing cost of the system with just one light source. The advantage of producing an optical system for simultaneously emitting a plurality of light beams without requiring multiple light sources provides the motivation to combine the single light source of Ellerbrock with the apparatus of Sofield. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the single light source in the apparatus of Sofield, since Sofield teaches laser light sources, and the single light source of Ellerbrock is also a laser light source.

It would have also been obvious to one of ordinary skill in the art at the time of the invention to modify the optical detector of Sofield with the CCD array of Wohlstadter, In order to detect and spatially resolve simultaneous emissions of emitted light. The ability to simultaneously detect signals from a plurality of regions improves the efficiency of multiplexed assays, thereby providing the motivation to combine the teachings of Sofield and Wohlstadter. One of ordinary skill in the art at the time of the invention

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would have also had a reasonable expectation of success in combining the teachings of Sofield and Wohlstadter since Sofield teaches light detection and the CCD array of Wohlstadter is one type of sensor that can detect light. As to claims 73 and 101, the detector array is configured to simultaneously detect the position of each of the microsensors in real time since Wohlstadter teaches that the CCD array detects and spatially resolve simultaneous emissions of emitted light. As to claims 74 and 102, Wohlstadter teaches that the detector is a CCD array. As to claims 82 and 109, in modifying the Sofield invention, the Wohlstadter CCD array has the same capability as that claimed by Applicant, i.e., it can detect the position of each of the microsensors by detecting movement of beams of light reflected by each of the microsensors.

Also, neither Sofield, Ellerbrock, nor Wohlstadter teach inlets and outlets in each well.

Pfost teaches a control and delivery system that provides fluids and reagents to each reaction well, in order to increase the efficiency and quantity of tests that can be performed simultaneously. See column 1, lines 22-62; column 6, line 47 to column 7, line 5; and Figure 9. (9) The system includes a plurality of wells 30 which are used to hold the reagents, solid supports, particles, and/or other materials in order for them to react to create products. Each of the reaction wells 30 has one or more entrance channels 32 and one or more exhaust or drain channels 34. See column 6, lines 13-21.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the apparatus of Sofield, Ellerbrock and Wohlstadter with a control

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and delivery system that provides fluids and reagents to each reaction well, as taught by Pfost, in order to increase the efficiency and quantity of tests that can be performed simultaneously. The benefit of increased efficiency and quantity allows a greater number of tests to be performed with automation, which provides the motivation to combine the teaching of Pfost with the teachings of Sofield, Ellerbrock, and Wohlstadter.

One of ordinary skill in the art at the time of the invention would also have had a reasonable expectation of success in combining the control and delivery system with the micro-cantilever structures, since the structures are capable of handling small quantities of fluid and reagents, and the control and delivery system is optimized for small quantities of fluid and reagents. Moreover, Pfost teaches that the device can be formed from glass, silica, quartz, plastics, polymers or the like, upon which reservoirs, channels and reaction cells can be formed (col. 6, lines 32-41.) Pfost also teaches that the device can incorporate optical elements for detection (col. 11, lines 41-55.) Thus, the skilled artisan would have had reasonable expectation of success in modifying the Sofield device according to the teachings of Pfost since the teachings of Pfost are compatible with an optical detection system, such as that of Sofield.

In regards to claims 69, 85-87 and 97, Sofield teaches a cross strip (15) that is equivalent to the claimed ridge since it prevents element (14), which is equivalent to the reflective paddle portion from bending. See page 2, paragraph 0019 and Figure 1. The cross strip (15) (equivalent to the claimed ridge) is thus “on” or “running around at least” a bottom and top portion of element (14) (reflective paddle).

In regards to claims 72, 83 and 100, Ellerbrock teaches a coupler array 210 with parallel beams 212. See column 5, lines 43-50 and Figure 2.

In regards to claims 77 and 105, Wohlstadter teaches a different binding agent at each discrete binding domain, in order to perform a multiplexed assay. See column 5, lines 2-4.

In regards to claims 79 and 106, Sofield teaches that the light source can come from underneath the glass bottom See page 2, paragraph 0022 and Figure 3.

In regards to claims 80 and 107, since an array with individualized fluid cells is involved, there necessarily needs to be a system to dispense fluid into the cells with the ability to control the amount.

In regards to claim 84, Sofield teaches that beam 28 hitting the bottom surface of the glass substrate at regions where micro-cantilevers are located will be transmitted through, hitting the regions where the silicon layer is on top of the glass substrate will cause the beam to reflect.

In regards to claim 89, Sofield teaches that the micro-cantilevers can be made of silicon nitride. See page 1, paragraph 0006.

As to claims 88 and 90-91, Sofield, Ellerbrock and wohlstadter do not teach that the glass portion is polydimethylsiloxane (claim 88) and that the fluid cell has an inlet and an outlet and at least one channel having a through hole formed in the silicon portion of the assembly (claims 90-91). Pfoest teaches polydimethylsiloxane as a substrate layer, in order to provide a material that is moldable and compatible with the types of samples and reagent fluids used for biological assays. See column 16, lines

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25-33. It would have been obvious to one of ordinary skill in the art at the time of the invention to replace the glass substrate of Sofield, Ellerbrock Wohlstadter with polydimethylsiloxane, as taught by Pfost, in order to provide a material that is moldable and compatible with the types of samples and reagent fluids used for biological assays. By having both beneficial characteristics of being moldable and biocompatible provides the motivation to combine the teaching of Pfost with the teachings of Sofield, Ellerbrock and Wohlstadter. One of ordinary skill in the art at the time of the invention would also have had a reasonable expectation of success in combining PDMS with the apparatus of Sofield, Ellerbrock and Wohlstadter, since the apparatus bottom is glass, and PDMS is one type of glass material.

As to claim 92, the inlet as discussed above with regard to claim 64 is equivalent to the claimed through hole for functionalization of the individual fluid reservoirs and the outlet as discussed above is equivalent to the claimed channel for introducing a fluid sample into the individual reservoirs.

Claims 75 and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sofield et al. (US 2002/0072127) in view of Ellerbrock et al. (US 6,204,920) and Wohlstadter et al. (US 6,066,448), and Pfost (6,485,690), as applied to claim 64 above, and further in view of Quate et al. (US 6,203,983) (hereinafter "Quate").

Sofield, Ellerbrock, Wohlstadter and Pfof have been disclosed above, but fail to teach that the optical detector array is a CMOS array.

Quate teaches a CMOS microelectric processing system, in order to easily integrate with silicon-based micromechanical devices such as cantilevers and to produce seamless sensors at low cost and integrate them directly into computers. See column 2, lines 11-23.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the system of Sofield, Ellerbrock and Wohlstadter with a CMOS microelectric processing system, as taught by Quate, because the CMOS detectors are low cost, can be easily integrated into computers, and can be utilized with silicon-based cantilevers. The ease of use and economic incentive provide the motivation to combine the teaching of Quate with the teachings of Sofield, Ellerbrock and Wohlstadter. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a CMOS system with a micro-cantilever structure array since the CMOS system can be integrated with silicon-based cantilevers and the micro-cantilever structures are silicon-based.

Claims 76, 81, 104 and 108 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sofield et al. (US 2002/0072127) in view of Ellerbrock et al. (US

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6,204,920) and Wohlstadter et al. (US 6,066,448), and Pfof (6,485,690), as applied to claim 64 above, and further in view of Lee et al. (US 5,807,758) (hereinafter "Lee").

The teachings of Sofield, Ellerbrock, Wohlstadter and Pfof are disclosed above, but fail to teach that at least one microsensor that is not functionalized to deflect when exposed to the target molecules.

Lee teaches a reference cantilever 82 in proximity to a modified cantilever 12, in order to eliminate sources of noise, including non-specific binding. See column 8, lines 44-64 and Figure 8.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the micro-cantilever structures of Sofield, Ellerbrock, Wohlstadter and Pfof by placing a reference cantilever in proximity to a modified cantilever, as taught by Lee, in order to eliminate sources of noise, including non-specific binding. This allows a clearer detection of sample binding on the functionalized micro-cantilevers, thereby providing motivation to combine the teachings of Lee with the teachings of Sofield, Ellerbrock, Wohlstadter and Pfof.

In regards to claims 81 and 108, Lee teaches that the cantilever can be detected using an interferometer. See column 8, lines 31-40.

Response to Arguments

Applicant's arguments filed January 4, 2007 have been fully considered but they are not persuasive. Applicant states that the claims have been amended to include the

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limitations "wherein each of the individual fluid cells has an inlet and an outlet", and Applicant argues that neither Sofield nor Ellerbrock nor Wohlstadter suggest or teach this limitation. Applicant also argues that although Pfoest suggests a fluid cell or well having an inlet and outlet, there is no reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed, since Pfoest does not teach, suggest or provide any motivation to provide a fluid cell having an inlet and outlet, or channel and through hole, which is compatible with an optical beam source configured to simultaneously direct an optical beam onto each of the microsensors in the array of microsensors, and an optical detector array configured to simultaneously detect the position of each of the microsensors.

This argument is not persuasive as Pfoest teaches that the device can incorporate optical elements for detection (col. 11, lines 41-55) and thus the skilled artisan would be suggested to modify the Sofield device such that the device has inlet and outlet channels. It would have been within the skills of the ordinary artisan to provide such inlets and outlets as taught by Pfoest in the Sofield device such that the Sofield device can still provide for the optical detection disclosed by Sofield since Pfoest teaches that the substrate upon which the reaction wells and inlets and outlets are formed can be made of glass (col. 6, lines 32-41) and thus transparent to light for providing a light source and detectors as taught by Sofield.

Applicant also argues that none of the cited references teach or suggest an array of microcantilever beams, wherein each of the microcantilever beams is comprised of a cantilever beam and a reflective paddle, the reflective paddle portion including a

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strengthening ridge, which prevents the reflective paddle portion from bending.

Examiner notes however that Applicant does not recite specific limitations regarding the structure of the strengthening ridge and reflective paddle portion such that they are distinguished from the structures disclosed by Sofield because cross strip (15) is equivalent to the claimed ridge since it inherently prevents the reflective paddle portion (14) from bending as can be inferred from the structure depicted in figure 1.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANN Y. LAM whose telephone number is (571)272-0822. The examiner can normally be reached on Mon.-Fri. 10-6:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ann Y. Lam/
Primary Examiner, Art Unit 1641